The Pending Claims

Claims 1-6 are pending and directed to the plasmid (claims 1-3), the transformant comprising the plasmid (claims 4 and 5), and the method of producing an enzyme through use of the plasmid (claim 6).

The Office Action

The Office has objected to the specification on the grounds that the title is not sufficiently descriptive. The Office has objected to claim 1 because the abbreviation, PQQ, is used without definition, and for the use of the nonstandard English phrase "defected of conjugative transfer function beforehand." Claims 1-6 have been rejected by the Office as allegedly indefinite under 35 U.S.C. § 112, second paragraph. The Office has rejected claims 1, 2, 4, and 6 under 35 U.S.C. § 102(b) as allegedly anticipated by Tamaki et al. (*Biochimica et Biophysica Acta, 1088,* 292-300 (1991)). Additionally, claims 1-4 and 6 have been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,103,509 (Sode et al.). The Office has rejected claims 1-6 under 35 U.S.C. § 103(a) as allegedly obvious in view of JP 11-243949 (Takeshima et al.) in combination with U.S. Patent No. 5,670,343 (Cameron et al.). Reconsideration of these rejections is hereby requested.

Discussion of Objection to the Specification

The Office has objected to the specification on the grounds that the title is not sufficiently descriptive. The title has been amended to more distinctly describe the claimed invention. Therefore, the objection to the specification based on the title should be withdrawn.

Discussion of Objection to Claim 1

The Office has objected to claim 1 because the abbreviation, PQQ, is used without definition, and for the use of the nonstandard English phrase "defected of conjugative transfer function beforehand." Applicants have amended claim 1 to include the definition of PQQ before the use of the abbreviation and to clarify the claim language. Accordingly, the objection to claim 1 should be withdrawn.

Discussion of the Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-6 have been objected to by the Office as allegedly indefinite. The claims have been amended to clarify the claim language without changing the scope of the claims. Accordingly, the section 112 rejection should be withdrawn.

Discussion of the Rejections under 35 U.S.C. §§ 102(b) and 102(e)

The Office has rejected claims 1, 2, 4, and 6 as allegedly being anticipated by Tamaki et al. (*Biochimica et Biophysica Acta, 1088,* 292-300 (1991)). Claims 1-4 and 6 have been rejected as allegedly anticipated by U.S. Patent No. 6,103,509 (Sode et al.). The Office has assumed that the vectors (pNK7 in the Tamaki reference and pTrc99A in the Sode patent) are broad-host-range vectors of the P-4 incompatibility group and are defective for conjugative transfer in the absence of evidence to the contrary by the Applicant (see page 4 of Office Action dated March 26, 2002).

The Tamaki and Sode references make no mention of these vectors lacking conjugative transfer function as required of the present invention as defined by the pending claims. Indeed, there is nothing in these cited references to suggest that the disclosed vectors lack conjugative transfer function. If anything, these cited references tend to suggest that the vectors possess the conjugative transfer function expected of such vectors in the normal course. In particular, the Tamaki reference describes the cloning and sequences of genes encoding two subunits forming the ADH complex of *A. polyoxogenes*, including preliminary experiments to determine a component necessary to exhibit ADH activity (see, e.g., page 292, col. 2, last paragraph, through page 293, col. 1, first paragraph). The purpose of the cloning experiments disclosed in the Tamaki reference cloning was to research the ADH complex and, thus, would not require the use of a vector which is nonconjugatable and nontransferable. Similarly, the Sode reference is directed to an enzyme protein, which is modified to have a substrate specificity to glucose. The expression vector, pTrc99A, which in Example 2 of the Sode reference is constructed to express the modified enzyme, is not described in terms of its conjugative transfer ability. In the absence of such a disclosure, the vectors disclosed in the Sode reference, as well as the Tamaki reference, must be presumed to be vectors with the normal complement of functions, including the conjugative transfer function.

Under the circumstances, neither the Tamaki reference nor the Sode reference satisfies each and every requirement of claim 1 or claims 2-6 dependent thereon. As such, the Tamaki and Sode references do not anticipate the subject matter of the pending claims, and the rejections of claims 1-4 and 6 under Sections 102(a) and 102(e) should be withdrawn.

Discussion of the Rejection under 35 U.S.C. § 103(a)

The Office has rejected claims 1-6 as allegedly being obvious in view of JP 11-243949 (Takeshima et al.) in combination with U.S. Patent No. 5,670,343 (Cameron et al.).

The Office contends that it would be obvious for one of ordinary skill in the art to alter the plasmid, pGLD3, of the Takashima reference to make the plasmid a non-mobilizable vector because the Cameron reference teaches the means to achieve non-mobilizable vectors by deletion of a region carrying a mob locus (see pages 5-6 of Office Action dated March 26, 2002).

It would not have been obvious, however, to apply the teachings of the Cameron reference to the plasmid of the Takashima reference, so as to prepare a broad-host-range plasmid that contains a gene coding for an enzyme taking PQQ as the prosthetic group and that is defective for conjugative transfer function. The reason the teachings of the Cameron reference would not be so readily applied to the plasmid of the Takashima reference is that the genes relating to replication, such as rep A, rep B, and rep C, as well as ori T, which is the starting point of the rep genes, are located near the mob gene. When mob genes are cleaved from vectors, portions of the DNA backbone near the mob genes often also are deleted as a result of experimental conditions, as well as the restriction enzymes. With the plasmid of the Takashima reference, the deletion of a portion of the DNA backbone near the mob gene could mean that the rep genes would be impaired, thereby causing a lower replication efficiency of the vector and lower expressed activity of the encoded enzyme. Accordingly, one of ordinary skill in the art would have expected that the removal of the conjugative transfer function in the plasmid of the Takashima reference by deletion of a region carrying the mob locus in accordance with the Cameron reference could lower the expressed activity of the enzyme, thereby tending to dissuade that ordinary artisan from doing so. There is nothing in either the Takashima reference or the Cameron reference that suggests otherwise.

The present invention surprisingly allows for a plasmid, wherein the expressed activity of the plasmid lacking conjugative transfer function, as assayed by the amount of enzyme produced by the plasmid, is comparable to the expressed activity of the same plasmid retaining conjugative transfer function. For example, the data in Table 2 of the specification indicates that 27 U/mL of expressed activity was recorded for *P. putida* TN1126/pGLD6 (pGLD6 lacks conjugative transfer function). The data in Table 1 of the Takeshima reference indicates that 26 U/mL (i.e., a comparable level) of expressed activity was recorded for *P. Putida* TN1126/pGLD3, wherein pGLD3 differs from pGLD6 solely by retaining conjugative transfer function (mob genes).

Under the circumstances, the present invention as defined by the pending claims must be considered unobvious over the disclosures of the Takashima and Cameron references. As such, the Section 103(a) rejection should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

John Kilyk, Jr., Reg. No. 30,763
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: June 24, 2002

In re Appln. of Hattori et al.
Application No. 09/765,865

CERTIFICATE OF MAILING

I hereby certify that this RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Date: June 24, 2002

PATENT
Attorney Docket No. 208753

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hattori et al.

Application No. 09/765,865

Filed: January 18, 2001

Art Unit: 1636

Examiner: B. Loeb

For: NOVEL PLASMID, BEARING THE PLASMID, AND METHOD OF PRODUCING AN ENZYME USING THE TRANSFORMANT

AMENDMENTS TO CLAIMS MADE IN RESPONSE TO OFFICE ACTION DATED MARCH 26, 2002

Amendments to existing claims:

1. (Amended) A plasmid [characterized in that the plasmid comprises] comprising a DNA fragment containing a gene coding for an enzyme taking pyrroloquinoline-quinone (PQQ) [PQQ] as the prosthetic group [as cloned in], wherein the plasmid is a broad-host-range vector [defected of] defective for conjugative transfer function [beforehand and that the plasmid is capable of being], and the plasmid is expressed in bacteria of the genus *Pseudomonas*.

4. (Amended) A transformant [characterized in that the transformant comprises] comprising the plasmid according to Claim 1 as introduced into a bacterial strain [capable of producing] that produces an enzyme taking PQQ as the prosthetic group.

5. (Amended) The transformant according the Claim 4 wherein the strain [capable of producing] that produces an enzyme taking PQQ as the prosthetic group is a bacterial strain of the genus *Pseudomonas*.

6. (Amended) A method of producing an enzyme taking PQQ as the prosthetic group, which method comprises [characterized by its comprising] growing the transformant according to Claim 4 in a nutrient medium to [let it] produce the enzyme taking PQQ as the prosthetic group in the culture broth and harvesting the enzyme taking PQQ as the prosthetic group from said culture broth.